Original Article

The lowest HU value on transverse planes: a predictive factor for cranial adjacent vertebral fracture risk after percutaneous vertebroplasty

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Background: Osteoporosis is the major risk factor for adjacent vertebral fracture (AVF). T-Score (DXAsp) cannot eliminate the confounding effect caused by pathological osteogenesis. Hounsfield unit (HU) values are credible predictors of bone density but cannot elucidate its regional differences. Since fracture occurs in the section with the lowest strength, HU values should be reliable predictors for AVF, and the predictive performance of the lowest HU in transverse planes should be better than those of other HU parameters. This study was designed to validate this hypothesis and to introduce an innovative parameter that can more accurately assess the incidence of AVF.

Methods: We conducted a retrospective review of prospectively collected imaging data from 103 patients diagnosed with a single segmental osteoporotic vertebral compression fracture (OVCF) who underwent percutaneous vertebroplasty (PVP) between July 2016 and August 2019. The average follow-up period for these patients was 24.1 months. T-Score (DXAsp) and HU values had been used to measure patients' bone density. HU was measured separately in the central transverse plane, the average values of three and four planes, and the lowest HU in transverse planes. Regression analyses identified independent risk factors for the cranial segmental AVF. We also performed receiver operating characteristic (ROC) curve analyses to assess the significant differences in predictive performances for different indicators.

Results: The overall incidence rate of AVF was found to be 26.21% (27 out of 103 cases). The HU values were significantly different; however, the T-Score (DXAsp) exhibited an insignificantly lower value in patients with cranial AVF following PVP. The area under the curve (AUC) values for four planes and three planes—average HU value, central transverse plane HU value, lowest HU value, and T-Score (DXAsp)—were recorded as 0.703, 0.705, 0.703, 0.765, and 0.57 respectively. Notably, the AUC of the lowest HU in transverse planes was significantly superior to that of the T-Score (DXAsp) and other HU measurement methods, with the exception of the central transverse plane HU value (P=0.118).

Conclusions: Compared to T-Score (DXAsp) and other traditional methods of HU measurement, the lowest HU value obtained from transverse planes demonstrates a superior ability to predict the incidence of AVF. Therefore, measuring this parameter is recommended for a more accurate assessment of AVF risk.

Keywords: X-ray computed tomography; osteoporotic vertebral compression fracture (OVCF); bone density; percutaneous vertebroplasty (PVP)

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Introduction

Osteoporotic vertebral compression fracture (OVCF) is one of the most common osteoporotic fractures in older patients (1,2). The clinical efficiency of percutaneous vertebroplasty (PVP) has been verified by several studies (3,4). However, with the growing application of PVP, the complication of adjacent vertebral fracture (AVF) has been repeatedly reported; AVF leads to severe back pain recurrence and an increased spinal sagittal imbalance, thereby affecting patients' quality of life (5,6). Osteoporosis progression (i.e., progressive reduction of bone density) is the major risk factor for AVF (5,7). The compressive strength of vertebral bodies decreases with bone density reduction, which is the pathological basis of OVCF caused by low-energy trauma (8,9). Traditionally, dual-energy X-ray absorptiometry (DXA) is the gold standard for osteoporosis diagnosis, but its inherent limitations may lead to AVF underestimation. For example, spinal degenerative diseases (SDD) are common in older patients, and the false increase of bone density caused by pathological bone formation (e.g., osteophytes and zygapophyseal joint osteoarthritis) in SDD cannot be eliminated by DXA (10,11). The bone density of cancellous bone cannot be directly measured by DXA. Since cancellous bone compression is the primary pathological phenotype of AVF, damage to the cancellous microstructure rather than the cortical shell or posterior structures should be seen as the main reason for the higher risk of AVF. However, these pathological changes cannot be directly measured by DXA (10,11). Therefore, the increase in the T-Score (DXAsp) in patients with OVCF and SDD may lead to the underestimation of AVF risk.

Recently, the vertebral Hounsfield unit (HU) value has become a credible indicator for evaluating the cancellous bone density (10,11). The HU of vertebral bodies is measured separately at four planes: the midsagittal plane, central transverse plane, and transverse planes close to the superior and the inferior endplate (12,13). Presently, three standard methods are used to record HU, namely the central transverse plane value, the three planes' average value (average value of three transverse planes), and the four planes' average value (average value of both transverse and midsagittal planes) (*Figure 1*). When measuring HU, researchers can easily adjust the region of interest (ROI), and the confusion caused by pathological bone formations can be eliminated. Therefore, because HU can evaluate the bone density of cancellous bone separately, it is a better predictor of AVF than the DXAsp (10,14).

The existing HU measurement methods exhibit inherent limitations when assessing the risk of AVF. Specifically, our previously published study demonstrated that regional variations in bone density exist within the cancellous bone of vertebral bodies (11,15). In this investigation, we calculated the difference between the highest and lowest HU values in transverse planes of vertebral bodies, establishing this factor as an independent risk predictor for AVF. According to fundamental principles of fracture mechanics, fractures tend to occur in regions characterized by lower bone strength (16,17). Furthermore, in studies addressing screw loosening, it has been shown that the density along screw trajectories serves as a more reliable predictor for screw loosening compared to overall vertebral body density (11,18).

Given that HU measurements taken at specific planes do not accurately reflect the lowest bone density within vertebral bodies and may obscure potential fracture risks—particularly in cases where there are significant regional differences in bone density—we hypothesize that identifying the lowest HU value across transverse planes adjacent to PVP segments would provide a superior prediction model for AVF compared to conventional methods that directly assess minimum bone density within vertebral bodies. The primary objective of this study was to validate this hypothesis and introduce an innovative parameter that can

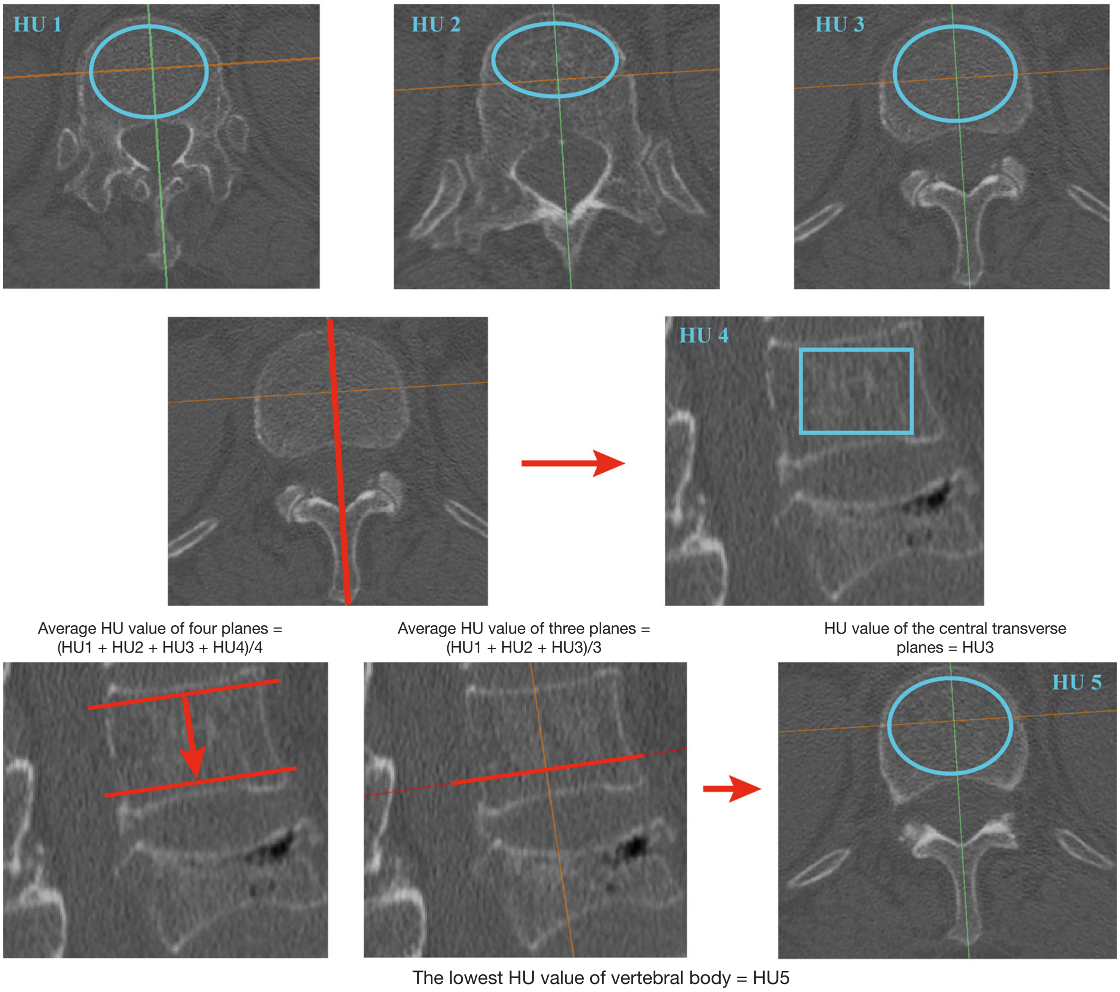

Figure 1 Schematic for different HU measurement methods. We measured HU values from five distinct planes: the central transverse plane, the sagittal plane, the transverse plane inferior to the superior bony endplate, the transverse plane superior to the inferior endplate, and the transverse plane with the lowest HU value. During this process, we calculated the average HU values for four of these planes (excluding that of the lowest HU value) as well as for three transverse planes. Based on similar studies in this field, it was determined that the average HU value from four planes, along with those from three planes and specifically from the central transverse plane, are commonly selected metrics to represent patients' bone density within vertebral bodies. These methods of measuring HU have been established as standard practices and are widely utilized in comparable research. Moreover, HU values of transverse planes were separately measured from the superior to the inferior BEP along the direction of red arrow, the lowest HU value of these transverse planes was defined as the lowest HU. Blue areas defined the ROI of HU values measurement, red lines defined the central sagittal plane and the transverse plane regions of HU values measurement. HU, Hounsfield unit; BEP, bony endplate; ROI, region of interest.

more accurately assess the incidence of AVF. We present this article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-24-1559/rc).

Methods

Patient data collection

This study was conducted in accordance with the

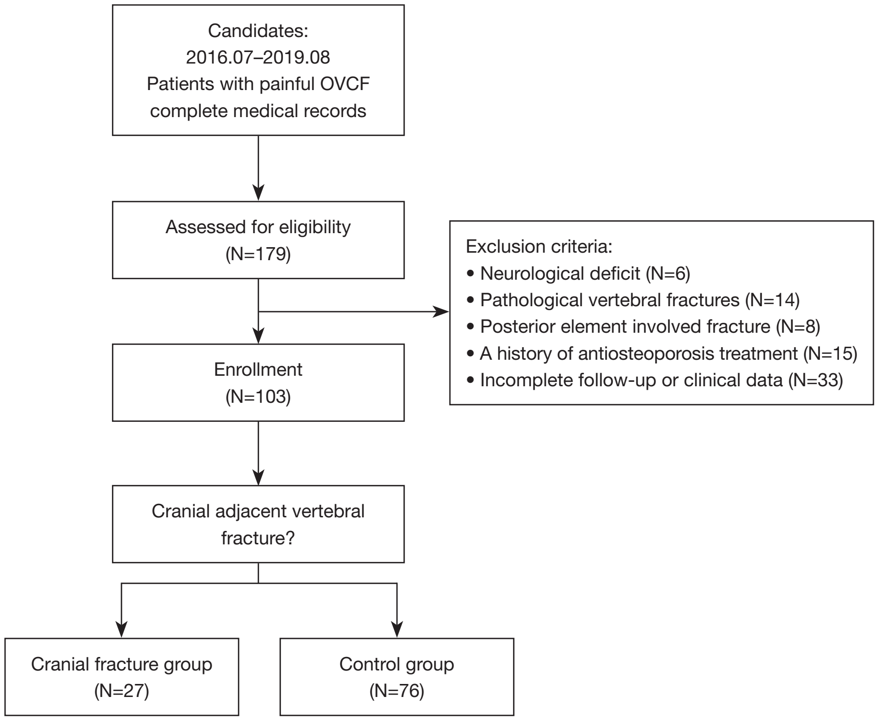

Figure 2 Schematic for patient inclusion and exclusion. OVCF, osteoporotic vertebral compressive fracture.

Declaration of Helsinki (as revised in 2013). Approval for the current study protocol was provide by the Ethics Committee of the Affiliated Hospital of Integrated Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine (No. 2022-LWKY-020). The informed consent requirement was waived because of the retrospective nature of this study. We retrospectively reviewed the prospectively collected demographic and radiographic data of 103 patients from Affiliated Hospital of Integrated Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine with one segmental OVCF who underwent PVP between July 2016 and August 2019. The average follow-up period of patients was 24.1 months (ranging from 22 to 25.5 months; both the sample size and follow-up period in the current study are superior to those found in most of comparable investigations). A senior spine surgeon performed the bilateral transpedicular PVP operations on these patients. Polymethylmethacrylate (PMMA) bone cement was used for all operations.

The inclusion criteria were as follows: (I) patients with severe back pain due to acute (<2 weeks) or subacute (between 2 and 8 weeks) OVCF; (II) patients with complete medical records and related radiographic data, including data on bone cement volume, preoperative CT scan; (III) patients with nearly 2 years' follow-up and complete clinical data. The exclusion criteria were as follows: (I) patients with a neurological deficit; (II) patients with pathological vertebral fractures caused by malignancies or infections; (III) patients with unstable fractures due to posterior element involvement; (IV) patients with a history of antiosteoporosis treatment [poor bone mineral density (BMD) is the most significant factor contributing to AVF progression (5,7). By employing consistent patient inclusion criteria, we can achieve relatively credible conclusions. Consequently, patients receiving individualized anti-osteoporosis therapy were excluded from this study]; and (V) patients with incomplete follow-up or clinical data [e.g., patients who underwent the preoperative computed tomography (CT) scan in another hospital] (*Figure 2*). The HU values obtained through various measurement methods and T-Score (DXAsp) were documented in this study to evaluate their potential predictive performance in predicting the incidence of AVF.

Assessment of AVF and HU measured using different methods

The measurements of these imaging data were independently performed by an experienced spine surgeon trained in imaging measurements. Patients who reported recurrent low back pain with a hypointense signal on T1-weighted images and a hyperintense signal on short tau inversion recovery (STIR) images of adjacent vertebral bodies and patients with a decrease in the height of the adjacent vertebral bodies as revealed by sagittal CT were provided a diagnosis of AVF (4,16). Since AVF mainly occurs in the vertebral body cranial to the cement augmented segment, HU values and AVF status in this segment were enrolled in this study (4,16).

HU values of vertebral bodies cranial to the PVP segment were measured using the preoperative CT imaging data under an identical definition. In this process, all patients were scanned using a 64-slice spiral CT (GE Healthcare, Chicago, IL, USA) scanner. CT scan parameters were presented as follows: slice thickness of 1 mm, slice spacing of 1 mm, tube voltage of 120 kVp, automated exposure control tube current of 300 mA (Smart mA/auto mA range, 150 to 750), the field of view: 50 cm, in-plane pixel size of 0.98×0.98, and a bone reconstruction algorithm (window width/window level, −3,000/300) (11,18). ROI was expanded to the largest area within the cancellous bone, but other bony structures, such as the cortical, bony endplates, osteophytes, and posterior venous plexus, were excluded.

This study measured HU values from five distinct planes: the central transverse plane, the sagittal plane, the transverse plane inferior to the superior bony endplate, the transverse plane superior to the inferior endplate, and the transverse plane with the lowest HU value. During this process, we calculated the average HU values for four of these planes (excluding that of the lowest HU value) as well as for three transverse planes. Based on similar studies in this field, it was determined that the average HU value from four planes, along with those from three planes and specifically from the central transverse plane, are commonly selected metrics to represent patients' bone density within vertebral bodies. These methods of measuring HU have been established as standard practices and are widely utilized in comparable research (3,10). Moreover, the lowest HU value of transverse planes was defined as the lowest HU (*Figure 1*). The CT scan thickness and HU measurement methods employed for all enrolled patients were entirely consistent.

Statistical analyses

Descriptive statistics and analyses of significant differences in bone density were performed using the statistical software SPSS 23.0 (IBM Corp., Armonk, NY, USA). Additionally, the significance of differences in area under the curve (AUC) values among various imaging-based parameters was assessed using R software (version 4.1.1; the R Foundation for Statistical Computing, Vienna, Austria). To judge the interobserver and intraobserver reliability, 10 patients were randomly selected. One week after imaging data measurement, imaging data of these selected patients were remeasured by the spinal surgeon and an experienced radiologist. The intraclass correlation coefficient (ICC) was computed to identify the repeatability of measured of HU values in the central transverse planes. When comparing the difference between patients in the two groups (with and without AVF), the independent sample Student's *t*-test was used for different HU measurement methods separately (15,19). Finally, we performed receiver operating characteristic (ROC) curve analyses to assess the predictive value of HU measured by different methods (20,21). The AUC was calculated and used as an indicator to judge the predictive performances. Differences in AUC have previously been compared between the DXAsp and HU measurement methods (22,23). An indicator is defined as a cut-off value when the sum of its sensitivity and specificity reaches its maximum (24,25).

Results

Patient characteristics and significant difference verification

A total of 103 patients with OVCF (78 women and 25 men) and an average age of 74.16±8.16 years were included in this study. The overall incidence rate of cranial AVF was 26.21% (27/103), and the average duration from the initial vertebral augmentation to the occurrence of AVF was 16.47±6.23 months. The inter-and intra-observer reliability of the variable measurements demonstrated excellent consistency, with ICCs of 0.864 and 0.823, respectively, when assessing the HU values in the central transverse plane. When it comes to the significant difference computation, the HU values measured by four different methods were significantly lower in the AVF group. However, there was no significant difference in the DXAsp between patients with and without AVF. Additionally, the mean HU values in patients without AVF were significantly higher than those in patients with AVF, and the results were not dependent on the HU measurement method. Additionally, differences

Table 1 Significant computation of bone density assessed by various methods in patients with and without AVF

BMD measurement methods	AVF	Without AVF	P value
HU (average of four planes)	69.39±26.48	82±23.61	0.001**
HU (average of three planes)	61.88±25.8	83.13±23.04	0.001**
HU (central transverse plane)	59.39±32.93	80.78±27.32	0.001**
HU (lowest value of vertebral body)	41.75±26.33	66.37±24.03	<0.001**
T-score	−2.26±1.59	−2.09±1.14	0.553

Data are presented as mean ± SD. **, statistical significance in the multivariate regression analysis (P<0.01). AVF, adjacent vertebral fracture; BMD, bone mineral density; HU, Hounsfield unit; SD, standard deviation.

in mean HU values in patients with and without AVF were 18.64, 18.25, 21.41, and 24.62 for the HU values measured at four planes, three planes, and the central transverse planes and the lowest HU in transverse planes, respectively. In other words, the HU difference between the two groups was higher at the lowest HU in transverse planes than at other planes (*Table 1*).

We performed ROC curve analyses to assess the predictive value of different independent risk factors for AVF (*Figures 3,4*). The AUCs of the DXAsp, four planes' average HU value, three planes' average HU value, the central trans plane's HU value, and the lowest HU value of vertebral bodies were 0.57, 0.703, 0.705, 0.703, and 0.765, respectively. In other words, the AUC of the lowest HU in transverse planes was numerically higher than other bone density evaluation parameters. A parameter with an AUC value greater than 0.7 demonstrates credible predictive performance when forecasting a specific outcome. Given that all HU measurement methods yielded AUC values exceeding 0.7 in predicting the risk of AVF, it can be concluded that HU values possess reliable predictive capability. Moreover, the AUC value of the DXAsp was significantly lower than that of all HU value measurement methods, and the AUC value of the lowest HU in transverse planes was significantly higher than the DXAsp and other HU measurement methods except for the central transverse plane's HU values (P=0.118). There were no significant differences in AUC between the three traditional HU measurement methods. The AUC of all HU measurement methods was significantly higher than the DXAsp (*Table 2*).

Discussion

Osteoporosis is an essential risk factor for fractures (26,27). Potential risk factors for AVF have been widely investigated. Although some studies have reported no significant difference in bone density between patients with and without AVF (28,29), most researchers still believe that osteoporosis progression is the initial trigger for AVF (2,30). Studies with negative results (i.e., low bone density did not increase the risk of AVF) have measured patients' bone density using DXA (12,31). The negative results may be because DXA cannot eliminate the confounding effect caused by pathological bone formation (14,32). Since the compressive fracture of cancellous bone is the primary pathological process of AVF, direct measurements of the cancellous bone density should precisely predict the risk of AVF. Consistent with these studies, a lower DXAsp is not an independent risk factor for AVF, and there was no significant difference in DXAsp between groups with and without AVF.

By contrast, by adjusting the ROI, HU measurement could eliminate the confounding effect of pathological osteogenesis (11,15). However, traditional HU measurement methods still have their inherent limitations. Specifically, these methods cannot eliminate regional differences in the vertebral body's bone density. According to the basic principle of biomechanics, fracture in the vertebral body occurs at the position with the lowest bone density and corresponding bone strength. An indicator that directly reflects the lowest bone density of the vertebral body should more effectively predict AVF's risk (30,33). To verify these hypotheses, we compared the predictive performances of the lowest HU in transverse planes to other HU measurement methods. Consistent with published studies (34,35), lower HU values measured by three commonly reported methods were independent risk factors for AVF. Moreover, the lowest HU in transverse planes is an independent risk factor for AVF. Its predictive performance is significantly better than that of the DXAsp, and four and three planes HU values,

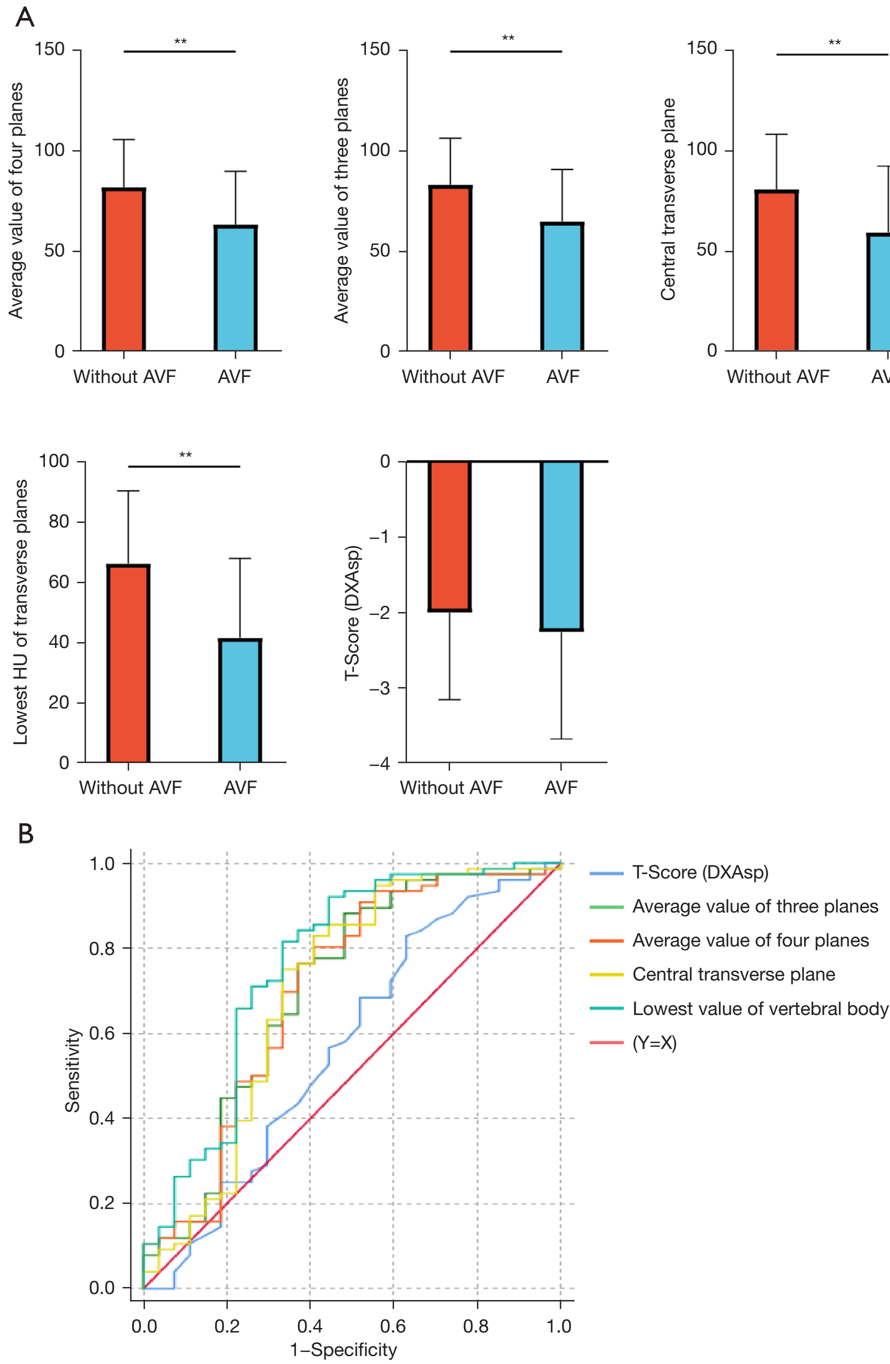

Figure 3 Computation of significant differences and ROC curves for HU values in patients with and without AVF. (A) Mean HU value measured using the four methods in patients with and without AVF: the HU values measured by four different methods were significantly lower in the AVF group. However, there was no significant difference in the T-Score (DXAsp) between patients with and without AVF. (B) ROC curves of different HU measurement methods: the AUCs of the T-Score (DXAsp), four planes' average HU value, three planes' average HU value, the central trans plane's HU value, and the lowest HU value of vertebral bodies were 0.57, 0.703, 0.705, 0.703, and 0.765, respectively. In other words, the AUC of the lowest HU in transverse planes was numerically higher than other bone density evaluation parameters. **, statistical significance in the multivariate regression analysis (P<0.01). AVF, adjacent vertebral fracture; HU, Hounsfield unit; DXA, dual-energy X-ray absorptiometry; ROC, receiver operating characteristic; AUC, area under the curve.

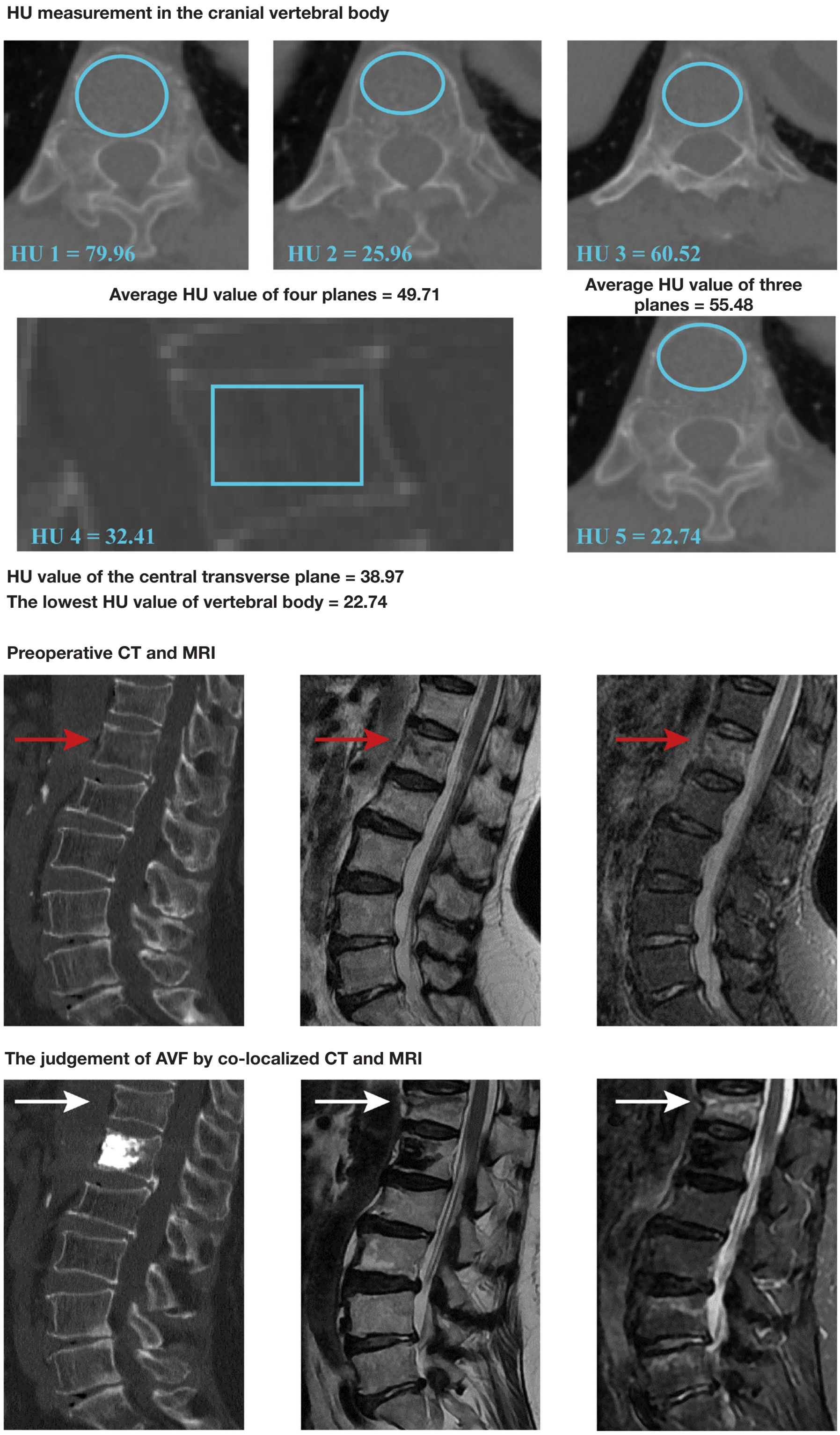

Figure 4 A typical case demonstrating the better predictive ability of the lowest HU in transverse planes in a patient with AVF. HU values have been measured in the marked ROI. Blue areas defined the ROI of HU values measurement, red arrow marked the fractured vertebral body in the first time, and the white arrow marked AVF cranial to the cement augmented vertebral body. HU, Hounsfield unit; AVF, adjacent vertebral fracture; CT, computed tomography; MRI, magnetic resonance imaging; ROI, region of interest.

Table 2 The cut-off value, sensitivity, and specificity for AVF prediction (AUC of the vertebral bodies' lowest HU value was higher than other HU measurement methods)

BMD measurement methods	Cut-off value	Sensitivity	Specificity	AUC
HU (average of four planes)	65.78	0.803	0.593	0.703
HU (average of three planes)	59.34	0.882	0.519	0.705
HU (central transverse plane)	58.12	0.829	0.593	0.703
HU (lowest value of vertebral body)	44.02	0.816	0.667	0.765
T-score (DXA)	−3.15	0.842	0.37	0.57

AVF, adjacent vertebral fracture; AUC, area under the curve; HU, Hounsfield unit; BMD, bone mineral density; DXA, dual-energy X-ray absorptiometry.

and numerically higher than HU in the central transverse plane. Therefore, the lowest HU value in transverse planes is a better predictor during the judgment of AVF in PVP patients.

In contrast, the AUC of lowest HU value was numerically, but insignificantly, higher than that of the central transverse plane (P=0.118); this negative result can be elucidated from two perspectives. Firstly, the limited sample size may contribute to this unfavorable outcome. More significantly, compared to the sub-endplate region, the central region of vertebral bodies typically exhibits lower BMD. Consequently, the HU values are often observed in this area, which may further explain the negative results when predicting the AUC value for both the lowest and central transverse planes in assessing the risk of AVF. Moreover, conventional CT-based HU measurement methods have been rapidly promoted in the judgment of cancellous density (15,33). However, quantitative computed tomography (QCT) is still the gold standard of imaging-based bone density measurement (36,37). QCT can accurately measure the bone density of the volume of interest; the accuracy of this method was still better than other commonly used methods when judging the bone density of a special region (36,37). In contrast, CT scan is a routine imaging test performed in OVCF patients. The HU measurement can be performed based on the CT imaging data without additional economic expense and radiation exposure. Based on current research, patients with poor HU values, especially poor HU in transverse planes, should be considered at higher risk for AVF. Therefore, we recommend that surgeons routinely assess the lowest HU value in the transverse plane. A reduction in this parameter should be considered a significant risk factor for an increased likelihood of AVF formation, thereby necessitating heightened vigilance towards these patients. Moreover, a decrease in the lowest HU value may also serve as a potential indication for prophylactic vertebral augmentation; however, it is essential to establish both the threshold for lowest HU values and the effectiveness of prophylactic treatment protocols in subsequent investigations. Besides, only four patients in the current series exhibited caudal side AVFs. In comparison to published studies (4,16), the incidence of AVF was significantly lower in the caudal vertebral body. Therefore, caudal AVF was not included in statistical analyses due to limited sample sizes.

From a methodological perspective, several topics warrant clarification. Firstly, the follow-up of asymptomatic patients was conducted via telephone and online platforms rather than in an outpatient department. This approach may have led to the oversight of some asymptomatic patients with fractures. However, based on our clinical experience and existing literature, it is well-documented that clinical symptoms in patients with OVCF are typically quite severe (38,39). Furthermore, there is currently no published data indicating a substantial population of asymptomatic OVCF patients. Therefore, we contend that our methods for patient follow-up do not significantly compromise the credibility of this study. Moreover, the incidence of AVF is influenced by various factors including cement distribution, volume injected during treatment, vertebral collapse and restoration status, as well as fracture locations (35,40). The primary focus of this study was to introduce an innovative imaging-based parameter rather than to identify risk factors associated with AVF. Consequently, although potential significance regarding these factors' impact on AVF incidence remains unexamined within this study's scope, we acknowledge that their confounding effects still exist. Nonetheless, we believe that these variables do not substantially undermine the reliability of our findings since

HU values were derived from a single series of patients (41,42). It remains essential to elucidate the potential significance of these factors concerning AVF incidence in future research endeavors.

Conclusions

Compared to DXAsp and other traditional methods of HU measurement, the lowest HU value obtained from transverse planes demonstrates a superior ability to predict the incidence of AVF. Therefore, measuring this parameter is recommended for a more accurate assessment of AVF risk.

Acknowledgments

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-24-1559/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-24-1559/coif). All authors report funding from the Project of National Clinical Research Base of Traditional Chinese Medicine in Jiangsu Province, China (No. JD2022SZXMS07), Scientific Research Project of Jiangsu Provincial Health Commission (No. M2022095), and the Seventh Batch of National Chinese Medicine Experts' Academic Experience Inheritance Work Project (No. 22QGSC6) to this manuscript. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Approval for the current study protocol was obtained from the ethics committee of Affiliated Hospital of Integrated Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine (No. 2022-LWKY-020). The informed consent requirement was waived because of the retrospective nature of this study.

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